PATENT SPECIFICATION (11) 1311060

1311060

NO DRAWINGS

(21) Application No. 341/72 (22) Filed 4 Jan. 1972

(31) Convention Application No. 108212 (32) Filed 20 Jan. 1971 in

(33) United States of America (US)

(44) Complete Specification published 21 March 1973

(51) International Classification A61K 7/00

(52) Index at acceptance

A5B 771 772

(19)

(54) COMPOSITION FOR THE AMELIORATION OF MALODOURS

(71) We, WARNER-LAMBERT COMPANY, of 201 Tabor Road, Morris Plains, New Jersey 07950, United States of America, a corporation organised under the laws of the State of Delaware, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention is concerned with new compositions, such as mouthwashes, mints, breath sprays and the like, having included therein one or more selected compounds.

We have found that the odour-masking qualities of mouthwashes, mints, breath sprays, toothpastes and the like are unexpectedly enhanced by the addition of one or more of a selected group of compounds. These compounds, which we call "reodorants" are terpenes which are distinguished by their ability to enhance the odour-masking efficiency of other compounds, when the former are present in minor amounts.

The odour-masking properties or deodorant properties of flavours and fragrances are well known. Flower oils have well known odour-masking properties but, when used alone, give rise to peculiar and, in many cases, unpleasant sensations. It is, therefore, apparent that not every fragrance or flavour would be aesthetically acceptable in diminishing malodours nor, for that matter, capable of reducing them at all.

The reodorant compounds which we have found to be suitable for use in the compositions of the present invention are α - ionone, α - methyl - ionone, citral, geranyl formate and geranyl acetate, which are terpenes. It has been further determined that only a few terpenes possess reodorant qualities although, in large amounts, many terpenes can be described as flavours and perfumes.

Thus, according to the present invention, there is provided a composition for the amelioration of malodours, comprising a known deodorant composition with a minor content of at least one compound selected from α - ionone, α - methyl - ionone, citral, geranyl formate and geranyl acetate.

Determination of reodorant properties of various substances has been carried out both *in vivo* and *in vitro*. The results obtained using both methods show good correlation in measuring reodorant properties. The method of measuring reodorance in each case was organoleptic, i.e. panels of judges skilled in making such determinations were used to evaluate the effectiveness of compositions containing small amounts of compounds being tested for reodorant properties by estimating the strength and quality of certain odours.

Much evaluation has been done using *in vitro* techniques for the screening of potential reodorant compounds. A procedure for carrying out such tests was designed for evaluation of such compounds and their masking effect on strong sources of odour, such as saliva which has been incubated by ageing in a test tube, onion, garlic and tobacco smoke. Incubated saliva exhibits the characteristic and typical malodour found in the mouth generally referred to as "bad breath" or halitosis.

Incubated saliva was prepared as follows: whole saliva was collected from random donors, pooled and filled into test tubes (10 cc./tube) and incubated at 37°C. for 18 hours. The tubes were cooled and then capped.

Onion oil (commercially available) was prepared as an odour concentrate as follows: 2 cc. 95% ethanol; 2 cc. "Tween" 80; 0.1 cc. Onion Oil; q.s. water to 100 cc. of concentrate ("Tween" is a Registered Trade Mark). This stock solution was used to prepare dilute onion oil solutions containing 0.5 cc. stock+249.5 cc. water.

A natural garlic oil concentrate stock solution was prepared as follows:

2.0 cc. 95% ethanol
2.0 cc. Polysorbate 80
0.05 cc. garlic oil
q.s. water to 200 cc.

This concentrate provided 5 cc. to 245 cc. of water for use in test procedures.

Tobacco smoke odour was obtained by bubbling the smoke from 12 cigarettes through 400 cc. of 5% aqueous ethanol.

Two factors were considered to be of importance in defining a reordorant: the amount of a standard concentration of reodorant required to mask an odour and the volatility of the reodorant compound. The latter consideration is based on the possibility that the source of malodour is not destroyed so much as it is masked by the countervailing reodorant. The effectiveness of the reodorant is, therefore, partially dependent upon its ability to volatilise competitively with whatever malodour may be present.

The factors of effective concentration and volatility were determined for various possible reodorant compounds. Effective reodorant concentration is determined as follows:

Five stoppered bottles are provided with 1 cc. of standard malodorous material, previously described, together with 1, 2, 3, 4 or 5 cc. of the reodorant compositions to be evaluated. A test panel of judges indicates which are still malodorous and to what degree and those which have no odour.

Tests which show an area around which the odour seems masked are further defined by adding reodorant to comparable 1 cc. samples in 0.2 cc. increments, starting at the last previous concentration at which malodour was still perceptible, to determine at what concentration the malodour is masked. This value is the number of cc. of reodorant solution required to overcome the specific malodour.

A second factor which is considered in screening potential reodorant compounds is that of volatility. Tests are made of compounds, in combinations with known sources of malodour, to determine whether, under as nearly equal conditions as possible, effective amounts of reodorant reach the nose, as compared to particular malodours. Judge make evaluations of malodour and reodorant combinations, noting the time elapsed in minutes and 1/100 ths thereof at which the malodour is judged to be masked by the reodorant compound. This test may proceed for a maximum of ten minutes.

The two numerical values arrived at in accordance with the above methods are multiplied. Compounds producing a reodorant value of 50 do not possess reodorant activity as defined herein.

How this reodorant value is arrived at is shown in the following hypothetical table giving results of dilution of a source of malodour with a reodorant solution and the neutralising of a malodour with vapour from a reodorant:

	Dilution	Vapour Mixing*	Reodorant Value
Compound A	1.6	5.0	8.0
Compound B	2.0	10.0	20.0
Compound C	0.5	1.66	0.83

*Time is given in minutes and hundreths of minutes. (Example: 1 minute 15 seconds becomes 1.25 minutes).

This concept of reodorant properties marks a new point of departure for the development of approaches to overcoming the problems of odour masking and at least aesthetically improving breath odour. It is also clear from the screening tests set forth below that the compounds of the present invention also possess qualities which suggests including them in aerosol room fresheners and other compositions designed to combat unwanted odours.

The reodorant value which has been selected as indicating compounds with no appreciable reodorant activity is 50; possible reodorant activity as deflected in a reodorant value sufficiently low to warrant further investigation would be about 30 and any value appreciably lower would be unquestionably active.

Once the reodorant concept was formulated, it appeared that it would be merely a matter of selecting obvious flavours and fragrances as probable reodorants. This did not prove to be the case. There was no consistency discernable between those compounds which were pleasant smelling of themselves and their effectiveness as reodorants. Several compounds tested not only possessed no reodorant effectiveness but, when used to mask unpleasant odours, produced a resultant odour worse than the original unpleasant odour.

An example of this occurred when incubated saliva was mixed individually with cinnamic aldehyde and ambrettolide, both of which have pleasant fragrances but each of these in combination with incubated saliva resulted in a more objectionable odour than the incubated saliva alone. Other compounds with slight to neutral fragrances unexpectedly displayed exceptional reodorant qualities on testing. Sixty-seven possibilities were screened, with the result that eleven were found to have sufficient reodorant to warrant further experiment and the five compounds of the present invention have been shown to be superior reodorants.

A sampling of various terpenes is set forth below. The reodorant values were arrived at in accordance with methods described above.

Reodorant Value

Reodorant	Malodour Compound			
	Saliva	Onion	Garlic	Tobacco
Geranyl formate	12.21	4.87	18.00	5.50
Geranyl acetate	6.24	5.40	40.0	—
Geranyl propionate	43.0	50.0	50.0	50.0
Geranyl butyrate	32.26	38.25	42.0	50.0
Geraniol	33.44	50.0	50.0	50.0
Citral	16.17	7.36	13.22	14.50
α - Ionone	3.75	0.50	1.22	1.80
α - Methyl - Ionone	6.20	—	—	—
β - Ionone	50.0	—	—	—

It is apparent, from a comparison of the results, that adjacent homologues do not have any necessary relationship with respect to reodorance.

We do not wish to be bound by any explanation of the phenomenon of reodorance but it may be theorised that this quality of a compound is due either to an ability to block odour receptor sites in the olfactory epithelium or to low olfactory thresholds for the compound and possibly a combination of both. This latter quality is the ease of detection of the reodorant compound when present in combination with other odours.

Further tests using human subjects having mouth odour problems were carried out using α - ionone as the reodorant. A test panel of five trained judges were used to monitor the breath of participants as to its odour. The participants are out of the judge's sight and their breath is conveyed to the judge's nose *via* a standardised cylindrical glass tube. A lapse of at least 90 seconds between samplings was adhered to, to prevent olfactory fatigue.

The *in vivo* methods had been refined by use of multiple judgings and replicate judgings. In the latter, a subject just rated was resubmitted to the judges for a second time, unknown to them, and the two evaluations compared. Judges scored the same or within 1 point of the previous score on a 1 to 9 rating scale about 85% of the time.

Three hundred and eleven subjects were tested using three flavour bases in conventional mouthwash bases which have included in them one or three flavorants, that of Flavour I, Orange Juice and Mint. These three formulations were used as such and with additions of α - ionone in amounts of 100, 500 and 1000 parts by weight per million.

A base value of breath odour was established using a random sampling of the test population using a scale of 1 to 9 with 5 indicating neutral or nearly odourless state while a lesser number indicates increasingly pleasant, while above 5 the higher the number indicates increasingly unpleasant odour. The standard for 9 was the odour of incubated saliva.

The results of the tests showed that the flavoured mouthwashes without reodorant reduced breath odour to different degrees with mint the most effective, Flavour I less effective and orange juice the least so. The improvement in breath odour quality was further increased when the mouthwashes were provided with increased amounts of α-ionone. This was the result when α - ionone was added in concentrations of 100, 500 and 1000 parts by weight per million.

The following Examples, which are given for the purpose of illustrating the present invention, represent embodiments which have proven to be particularly effective for obtaining the best results in breath odour improvement through the use of reodorant compounds:—

Example 1

1. Glycerol USP	100.0	g.
2. Sorbitol Solution USP	40.0	g.
3. "Tween" 60 SD	6.0	g.
4. SD Alcohol 38-F[1)]	182.7	ml.
5. Sodium Cyclamate NF (optional)	1.6	g.
6. Saccharin Sodium NF Powder	0.16	g.
7. Flavour I[2)]	0.753	g.
8. FD & C Red #2 (100% dye)	0.6	mg.
9. FD & C Yellow #6 (100% dye)	10.0	mg.
10. Sodium Phosphate Dibasic Anhydrous	1.1	g.
11. Citric Acid Anhydrous USP, Fine Granular	0.72	g.
12. Water Purified USP	q.s. to 1000.0	ml.

1) Alcohol SD 38F

Boric Acid, USP Granulated	1.5100	g.
Menthol USP	0.5526	g.
Cassia Synthetic	0.0945	g.
Alcohol USP	180	ml.
Total Volume	182.7	ml.

2) Flavour I	
Cassia	0.44176 g.
Orange Juice F-4521	0.31114 g.
Lavandin Extra 30/32	0.00002 g.
Orange Flavour Absolute	0.00002 g.

Method for Preparation.

Step:

A. Add 3 to 4 and mix. Add 1 and 2. Continue mixing.

B. Add 7 and 8 to A, mix for 15 minutes.

C. Bring B to 95% of finished volume with 13. Add 5, 6, 11 and 12. Mix until solids have dissolved and continue mixing until solution clears (approx. 45 min.).

D. Bring C to volume with 13, mix well and allow to stand overnight at ambient temperature.

E. Filter.

F. Add 9 and 10 to E and remix.

The mouthwash prepared as set forth above was then provided with α - ionone as the reodorant in amounts of 100, 500 and 1000 parts per million by weight of composition. The resultant mouthwashes were judged to be more effective at improving the breath of various subjects according to a panel of judges using the organoleptic method earlier described. The mouthwash alone as well as the mouthwash plus the various amounts of reodorant and also the mouthwash above but with the flavour replaced by mint flavour in one set and orange juice flavour in another, were evaluated.

The combination evaluated were:

1. Mouthwash as in Example I+100 ppm α - ionone.
2. Mouthwash as in Example I+500 ppm α - ionone.
3. Mouthwash as in Example I+1000 ppm α - ionone.

Three compositions as in 1, 2 and 3 except that the flavour in each was changed to mint.

Three compositions as in 1, 2 and 3 except that the flavour in each was changed to orange juice.

Three compositions without reodorant but using Flavour I, mint and orange juice.

The qualitative evaluation of these 12 combinations of mouthwash bases without reodorant and with 100 parts per million, 500 parts per million and 1000 parts per million, with the Flavour of Example I, mint flavour or orange juice flavour were the following:

The combination having the greatest diminution of malodour was the mouthwash with mint flavour and 1000 parts per million reodorant followed by others in this descending order:

Flavour I	—1000 parts per million reodorant
Orange Juice Flavour	—1000 parts per million reodorant
Flavour I	— 500 parts per million reodorant
Mint Flavour	— 500 parts per million reodorant
Orange Juice Flavour	— 500 parts per million reodorant
Mint Flavour	—without reodorant
Orange Juice Flavour	— 100 parts per million reodorant
Flavour I	— 100 parts per million reodorant
Mint Flavour	— 100 parts per million reodorant
Flavour I	—without reodorant
Orange Juice Flavour	—without reodorant

It is generally apparent that the reodorant action of the compound increases with the increase in the amount present and that various flavours in compositions also effect their odour-masking abilities.

Reodorants have also been found useful in combination with chewing gum, pressed mint and candy lozenge formulations. The reodorant is usually supplied to these formulations in pure form and not in dilute solution. α - ionone is used in its pure form and not in dilute solution, its pure form being that of an oily liquid which is easily compounded with the usual ingredients of such material.

All amounts in the following examples are given in parts per weight:

Example II

Chewing Gum	
Gum base	20%
Sugar	64%
Corn Syrup	15%
Flavour	1%
Reodorant Compounds	10—1000 parts/million

Example III

Pressed Mint	
Sugar	94.75%
Corn Syrup	4%
Magnesium Stearate	1%
Flavour	0.25%
Reodorant Compounds	10 to 1000 parts/million

Example IV

Candy Lozenge	
Sugar	64%
Corn Syrup	35%
Flavour	1%
Reodorant Compounds	10 to 1000 parts/million

Reodorant compounds added within the ranges indicated do not change the finished product physically in any essential manner. The reodorant compound's qualities are unimpaired by the processes used for the preparation of these various compositions.

Example V

A preferred mouthwash composition is prepared as follows:

1. Glycerol USP	50.0000	g.
2. Sorbitol Solution USP	100.0000	g.
3. Alcohol SD 38B[3] for Reodorant Mouthwash W6680-25	253.2000	ml.
4. Sodium Saccharin NF Powder	1.2000	g.
5. Sodium Phosphate Dibasic Anhydrous	0.1600	g.
6. Sodium Phosphate Monobasic Crystalline	1.2000	g.
"Tween" 80 SD	15.0000	g.
8. Menthol USP	0.0040	g.
9. Imitation Mouth Refresher (9/702559)	1.0000	g.
10. Mouthwash Flavour V-30.278	1.0000	g.
11. α - ionone	1.0000	g.
12. FD & C Blue #1 (100% dye basis)	0.0020	g.
13. D & C Yellow #10 (100% dye basis)	0.0100	g.
14. Water, deicnised USP q.s. to	1.0000	L.

3) Alcohol SD 38B

1. Menthol USP	1.5960	g.
2. Peppermint Oil USP	1.4000	g.
3. Alcohol 95% USP	250.0000	ml.

Method of Preparation.

A. Add 7 to 3 and mix well.
B. Add 8, 9, 10 and 11 and mix well.
C. While mixing rapidly, slowly add 14 to approx. 1/2 of final volume. Mix until clear.
D. Add 1 and 2 to C and mix well.
E. Add 14 to 2/3 of final volume. Mix thoroughly.
F. Add and dissolve 4, 5 and 6 in E.
G. Q.S. to final volume with 14. Mix thoroughly.
H. Filter.
I. Determine volume of filtrate.
J. Add 12 as 0.1% aqueous solution adjusted to filtrate volume (theoretically 210 ml./1000 ml.).
K. Add 13 as 1.0% aqueous solution adjusted to filtrate volume (theoretically 1.0 ml./1000 ml.).
L. Mix thoroughly.

The resulting mouthwash was at least the equivalent to that of Example I, with mint flavour and 1000 ppm α - ionone, with respect to ameliorating breath odour. It has a clear, green appearance and has the odour and taste of spice mint. The taste is generally pleasing and lingers for some time after using.

We disclaim any use of the present invention in the United Kingdom which is contrary to the provisions of the Artificial Sweeteners in Food Regulations 1967.

WHAT WE CLAIM IS:—

1. A composition for the amelioration of malodours, comprising a known deodorant composition with a minor content of at least one compound selected from α - ionone, α-methyl - ionone, citral, geranyl formate and geranyl acetate.

2. A composition according to claim 1, wherein the reodorant is present in an amount, by weight, of from 10 to 2000 parts per million.

3. Compositions according to claim 1 for the amelioration of malodours, substantially as hereinbefore described and exemplified.

VENNER, SHIPLEY & CO.,
Chartered Patent Agents,
Rugby Chambers,
2, Rugby Street,
London, W.C.1.
Agents for the Applicants.

Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa, 1973.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.